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Early and Late Outcome, Mortality and Major Morbidity After Lung Cancer Surgery for Primary Carcinoma

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Abstract

Background: Radical surgical resection of lung cancer with or without adjuvant treatment is still a prerequisite for cure. Advances in operative and post-operative care led to a decline in complications and mortality rates during the last decades. Despite different additional modes of treatment, survival is still poor.

Objective: To examine the operative mortality and morbidity after lung cancer surgery and to identify factors associated with an adverse outcome.

Material and methods: The study consisted of 1017 consecutive patients, who were referred at the University Hospital of Lung Disease, "Shefqet Ndroqi," in Tirana, Albania, for lung carcinoma during a 15-year period (January 2004-December 2019). All patients underwent routine laboratory examinations, spirometry and preoperative CT-scan of the thorax and upper abdomen. PET-CT, EBUS–EUS, Mediastinotomy or Mediastinoscopy, were not routinely performed.

Results: Of 1017 patients, 718 (71.6%) were male and 299 (29.4%) were female. The mean age was 65.5±9.4 years (range 15-87 years). Lobectomy was the most practiced surgical modality in 634 (562.5%) patients. Meanwhile, pneumonectomy was performed in 113 (11.1%) patients. Minor complications during surgery occurred in 79 (7.7%) of patients. Continuous air leakage was the most prevalent complication after surgery, occurring in 25.3% of patients, followed by lung atelectasis in 22.8%, and cardiovascular complications in 16.4%.

Conclusion: Our results show low mortality and morbidity after lung cancer surgery. However, patients with reduced lung capacity, older age, and those undergoing pneumonectomy should be treated with great care.

Keywords: Outcome, complications, lung cancer, thoracic surgery.

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Introduction

Lung cancer is the most common form and cause of cancer-related deaths worldwide.

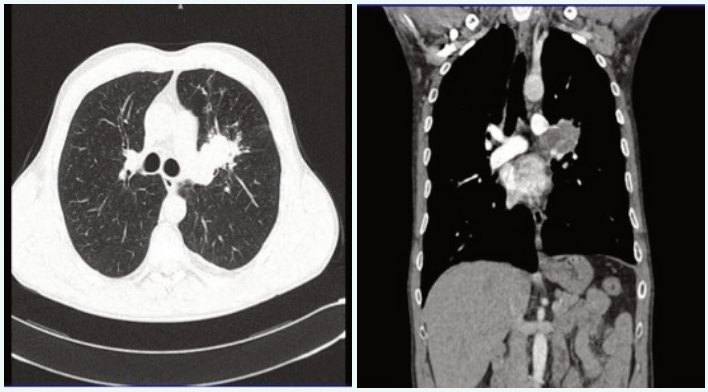


Figure 1: *Chest Ct-scan: Left upper lobe lung carcinoma*

In European countries, the proportion of patients who underwent surgery for this disease varied between 10 and 20%. Advances in operative and postoperative care have led to a decline in complications and mortality rates during the last two decades.[1] Despite different additional modes of treatment, survival is still poor. To be able to improve the quality of operative procedures, it is important to: identify patients running the highest risk, optimize the patient's condition, check medication and respiratory status before surgery, have knowledge of peri- and post-operative mortality and morbidity, and anticipate risk factors prior to surgery.

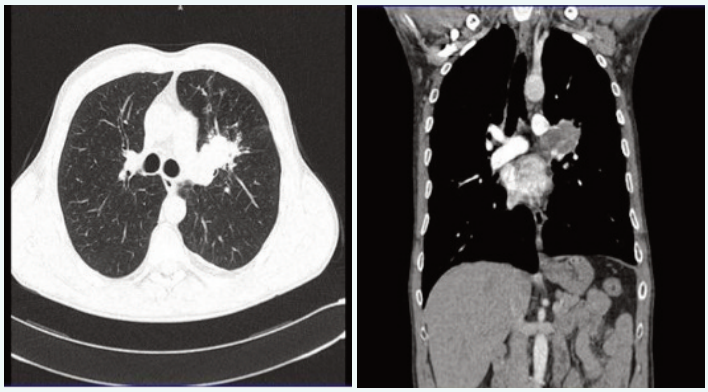


Figure 2: *Chest Ct-scan view of left upper lobe carcinoma; Macroscopic specimens*

Material and methods: The study consisted of 1017 consecutive patients, who were referred at the University Hospital of Lung Disease, "Shefqet Ndroqi," in Tirana, Albania, for lung carcinoma during a 15-year period (January 2004-December 2019). All patients underwent routine laboratory examinations, spirometry and preoperative CT-scan of the thorax and upper abdomen. PET-CT, EBUS–EUS, Mediastinotomy or Mediastinoscopy, were not routinely performed.

Staging of cancer is based on 8th edition of the TNM classification for Lung cancer (table below):

	N0	N1	N2	N3	M1a	M1d	M1c
T1a	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
T1b	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
T1c	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2a	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
T2b	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	IIIA	IIIA	IIIB	IIIC	IVA	IVB	IVB

Data are presented in numerical values and in percentages. Statistical processing was done with the Student test. The differences among the groups were called statistically significant for $p < 0.05$

Results

Of 1017 patients, 718 (71.6%) were male and 299 (29.4%) were female. The mean age of patients was 65.5±9.4 years (range 15-87 years), of which 291 (28.6%) patients were over 70 years. No differences were observed in death rates between the genders (female vs. male, 4.0% vs. 3.8% respectively; p=0.476).

Table 1: Demographic characteristics in relation to death within first 30 days of surgery and major complications

Patient characteristics in relation to death within first 30 days of surgery and major complications						
Complications		**Patients**	**Death within 30 days**		**Major complications**	
		N (%)	N (%)	P-value	N (%	P-value
Gender	Female	299 (29.4)	12 (4.0)	0.476	20 (6.7)	0.984
	Male	718 (71.6)	28 (3.8)		31 (4.3)	
Age	< 70 years	727 (71.4)	22 (3.0)	0.3	23 (3.3)	0.0024
	≥ 70 years	291 (28.6)	18 (6.1)		28 (9.6)*	
Comorbidity	Yes	277 (27)	23 (8.3)	0.064	32 (11.5)*	0.0001
	No	740 (73)	17 (2.2)		9 (1.24)	
Total		1017(100)	40 (3.9)		51 (5.0)	

According to histopathology, most patient results displayed squamous cell carcinoma (55.8%), followed by adenocarcinoma (34.4%). The remaining patients presented with other cancer types.

Significant differences in mortality within 30 days were seen between adenocarcinoma, squamous cell carcinoma, and other types of cancer (2,87%, 4.0% vs. 7.9% respectively; p< 0.01). Although major complications were observed in other groups of cancer, no significant differences were seen between groups. Over 2/3 of patients (78%) were current smokers, and only 22% never smoked. No significant statistical differences were seen in terms of death or major complications among the groups (3.8% vs. 4.0% and 10.0% vs. 5.8% respectively). Lung function was the parameter of particular importance as a prognostic factor in the evaluation of patients after surgery. A significant difference in patients was seen with FEV1<70% compared to those with FEV1>70% in terms of mortality and major complications (8.7% vs. 2.3% and 11.7% vs.2.6% respectively).

Table 2: Mortality and major complications, tumor, and patient characteristic, (nr. %)

	Patients , (N, %)		Mortality within 30-days, (N, %		Major complications Nr, %	
Histopathological type						
Adenocarcinoma	350	34.4	10	2.8	16	4.6
Squamous cell ca.	568	55.8	23	4.0	25	4.4
Other types	99	9.8	7	7.9*	109	10.1
Smoking habits						
Smoker	793	78	30	3.8	38	10.0
Never smoked	224	22	9	4.0	10	5.8
Lung function (FEV1, %)						
FEV1 > 70%	753	74	17	2.3	20	2.6
FEV1 < 70%	264	26	23	8.7**	31	11.7***

*statistically significant

It is noted that the largest number of patients belonged to stage III + IV (73%) of cases, compared to 27% in stages I + II. Single lobectomy significantly predominates versus other types of surgery. Lobectomy was the most used surgical modality in 634 (62.3%) patients. Meanwhile, pneumonectomy was performed in 113 (11.1%) patients.

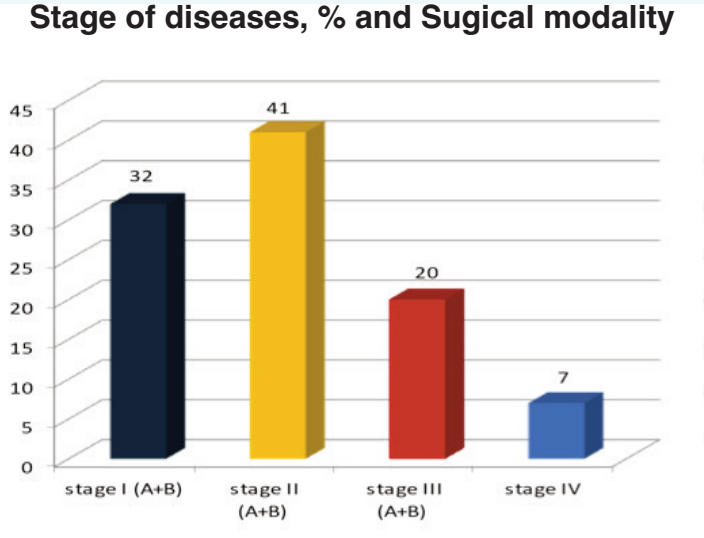


Figure 1: *Stage of diseases and surgical modality*

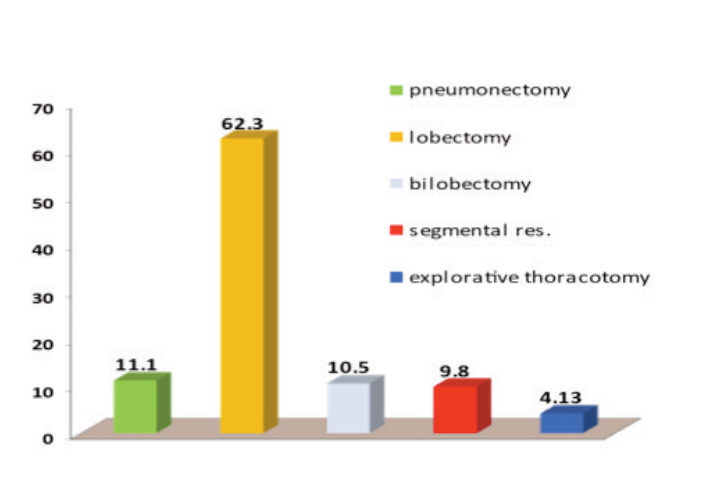


Table 3: Minor and major complications during surgery

In terms of minor complications, the largest number of cases present air leaks and postoperative pulmonary atelectasis consisting of almost half of the complications (¼ and 1/5 of all complications, respectively), followed by those of cardiac and obstructive syndrome (16.4% and 14.6%, respectively). While other complications occupy less than 10% of postoperative complications. Among the major complications, respiratory failure, bronchopleural fistulas, and pulmonary edema are the most common with over 50% of postoperative complications.

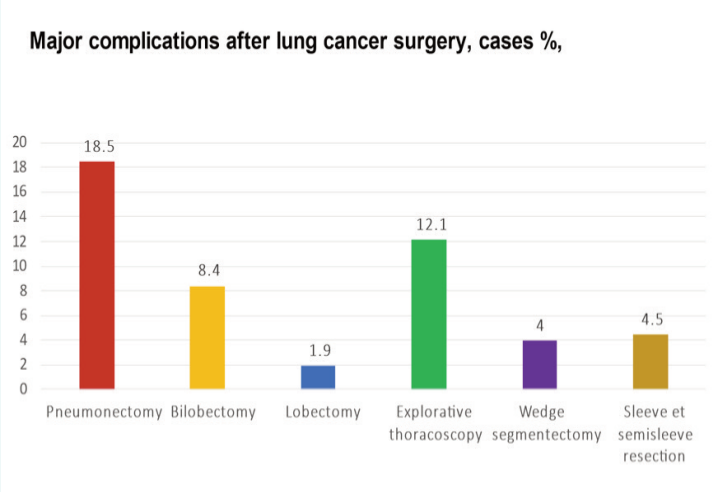
Minor and Major Complications within first 30 days after surgery, (7.7% vs.5.01%)

Minor complications	Nr.	%
Supraventricular arrhythmias	13	16.4
Continuous air leakage	20	25.3
Lung Atelectasis	18	22.8
Obstructive symptoms	11	14.6
Paresis of recurrent nerve	1	1.3
Insufficient wound healing	4	5.3
Diaphragmatic paresis	7	8.0
Mediastinal shift displacment	5	6.6
Total non-life-threatening disorder	79	100

Major complications	Nr.	%
Respiratory failure	11	21.5
Bronchopleural fistulas	9	17.6
Pulmonary edema	8	15.7
Cardiac failure	6	11.7
Tumor embolism	5	9.8
Myocardial infarction	3	5.9
Chilothorax	3	5.9
Postoperative bleeding	5	8.3
Cerebral infarction	1	2.0
Total	51	100

Univariate analysis of mortality and morbidity after lung resection surgery.

	Patients , (N, %)		Mortality within 30-days, (N, %)		Major complications Nr,	
Type of surgery 5.09%			40 3.9		Nr. 51	
Pneumonectomy	113	11.1	16	14.1	21	18.5
Right , P/ectomy	43	4.2	9	20.9	13	30.2
Left , P/ ectomy	70	10.0	7	10.0	7	10.0
lobectomy	634	62.5	8	1.3	12	1.9
bilobectomy	107	10.5	7	6.5	9	8.4
Explorative thoracotomy	41	4.1	4	9.0	5	12.1
Wedge, segmentectomy	100	9.8	2	2.0	4	4.0
Sleeve et semisleeve resection	22	2.1	1	4.5	1	4.5



Discussion

Currently, bronchial cancer represents a health problem all over the world. One third of all cases occurs in patients of around 70 years of age.[1] In our study, there have been 71.6% male and 29.4% female patients affected. This is closely related to the smoking habit, which is found to be widespread in males.[2]

We found differences in death rates observed between genders (female vs. male 4.0% vs. 3.8% respectively; p=0.476). In this study, the age of the intervening pulmonary carcinoma varied from 15 to 87 years. Of 1017 cases, 299 patients were over 70 years old. Mortality and major complications occurred with significant differences compared to those under 70 years old (p=0.03 and 0.0024 respectively). Nevertheless, old age alone does not appear to be a definite contraindication to surgery. There are surgical experiences in patients over 70 years of age, which indicate that this therapeutic strategy can be performed with good results.

Studies concluded that, in an elderly subject, not age, but rather the spread of disease and the cardio-pulmonary reserve should guide the choice of intervention. In addition, significant differences were seen in patients with comorbidity.[3,4]

Furthermore, previous studies have indicated that concomitant diseases such as ischemic heart disease, diabetes mellitus, or chronic obstructive lung disease represent significant risk factors for an adverse outcome.[5]

The histological examination of the material in this study shows the significant predominance of the squamous cell carcinoma and adenocarcinoma versus other types. However, based on the sex of the patients, predominance of adenocarcinoma is observed in females, due to an increase in the number of smokers. Surgical treatment of pulmonary cancer is the method chosen for stage I and II. Procedures that save pulmonary parenchyma offer lower mortality and morbidity than pneumonectomy and instability, when complete resection has taken place.[2,6-8]

Lung function is a parameter of particular importance as a prognostic factor in evaluation of patients after surgery. In this study, a significant difference in patients is seen with FEV1<70% as compared to FEV1>70% in terms of mortality and major complications (8.7% vs. 2.3% and 11.7% vs. 2.6% respectively). According to the extent of pulmonary resection, the largest number of cases is treated with lobectomy (62.5%) followed by bilobectomy and pneumonectomy (11.1%), and segmentectomy (9.8%); explorative thoracotomy [p <0.001] is performed less. As expected, the mortality rate was higher following pneumonectomy (14.1%) than other types of surgery.

The major complications, most often related to a

postoperative death, were respiratory failure (21.6%) followed by Broncho-pleural fistula in 17.6%, and pulmonary edema in 15.7% of patients.

These data are in accordance with other reports. In several studies, risk factors for major complications after lung resections have been identified, namely: age, male sex, smoking, and concomitant disease.[9-12] As confirmed in the present study, a low respiratory capacity, assessed as FEV1% and pneumonectomy, appears to be the most important predictor of a high risk of complications after lung resections. Our results confirm that low mortality (3.9%) and an acceptable level of major morbidity (5.09%) can be achieved after surgical resections for lung cancer, especially after single lobectomies (1.3%).

Conclusion

Our results show low mortality and morbidity after lung cancer surgery. However, patients with reduced lung capacity and those undergoing pneumonectomy should be treated with great care, as they run a considerable risk of major complications or death during the first 30 days postoperatively. Older age (>70 years) does not appear to be a contraindication to lung cancer surgery, but patients, included in this group, should undergo careful preoperative evaluation.

Conflict of Interest Disclosure Statement

The authors have no conflicts of interest to disclose.

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